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Microbiological investigation of polyarthralgia

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Abstract

Results of serological investigations on patients with joint pain, arthralgia or polyarthritis were analysed and this information was used to develop a diagnostic algorithm to ensure optimal utilisation of laboratory resources. Accordingly, all cases are now examined for parvovirus IgM, mycoplasma IgM and streptococcal antibodies. Further tests are undertaken by following the algorithm after obtaining supplementary information from a questionnaire. This approach is put forward as a preliminary standard which other laboratories may like to evaluate and develop according to local requirements.

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Keywords: Polyarthralgia, algorithm.

Selection of the appropriate serological investigations in patients with arthralgia often poses difficulty.^{1,2} To ensure the optimal use of resources and time, it is important that the relevant investigations are chosen from the wide range of available tests.

Methods

To determine the current practice in our laboratory, the results of the serology performed over the last six months on patients with a clinical history of joint pain were analysed. On the basis of these observations, guidelines for the future investigation of patients with polyarthralgia were prepared.

Results

The serological findings for the 140 patients studied are shown in the table. An outbreak of parvovirus infection coincided with this study and polyarthritis was attributed to this infection in one quarter of all patients investigated.

Four serum samples had antistreptolysin O (ASO) titres >800 units/ml and DNase antibodies above 300 units/ml. Six serum samples had ASO titres between 500 and 800 units/ml, all indicative of recent streptococcal infection. An additional two serum samples had raised anti-DNase antibodies with a normal ASO which, in the presence of a compatible clinical history, were also considered suggestive of a streptococcal illness. In total, 12 serum samples exhibited evidence of recent streptococcal infection—that is, 8.6% of all the patients studied.

The heterophil antibodies detected by the positive monolateral tests were not confirmed as recent Epstein-Barr virus (EBV) infections—that is, exhibiting a positive immunofluorescence test for EBV capsid antibody in the presence of a negative enzyme linked immunosorbent assay (ELISA) test for EB nuclear antigen antibody. In eight patients the positive monolateral test appeared to be related to the presence of recent infection with parvovirus, a difficulty that has been reported previously.³

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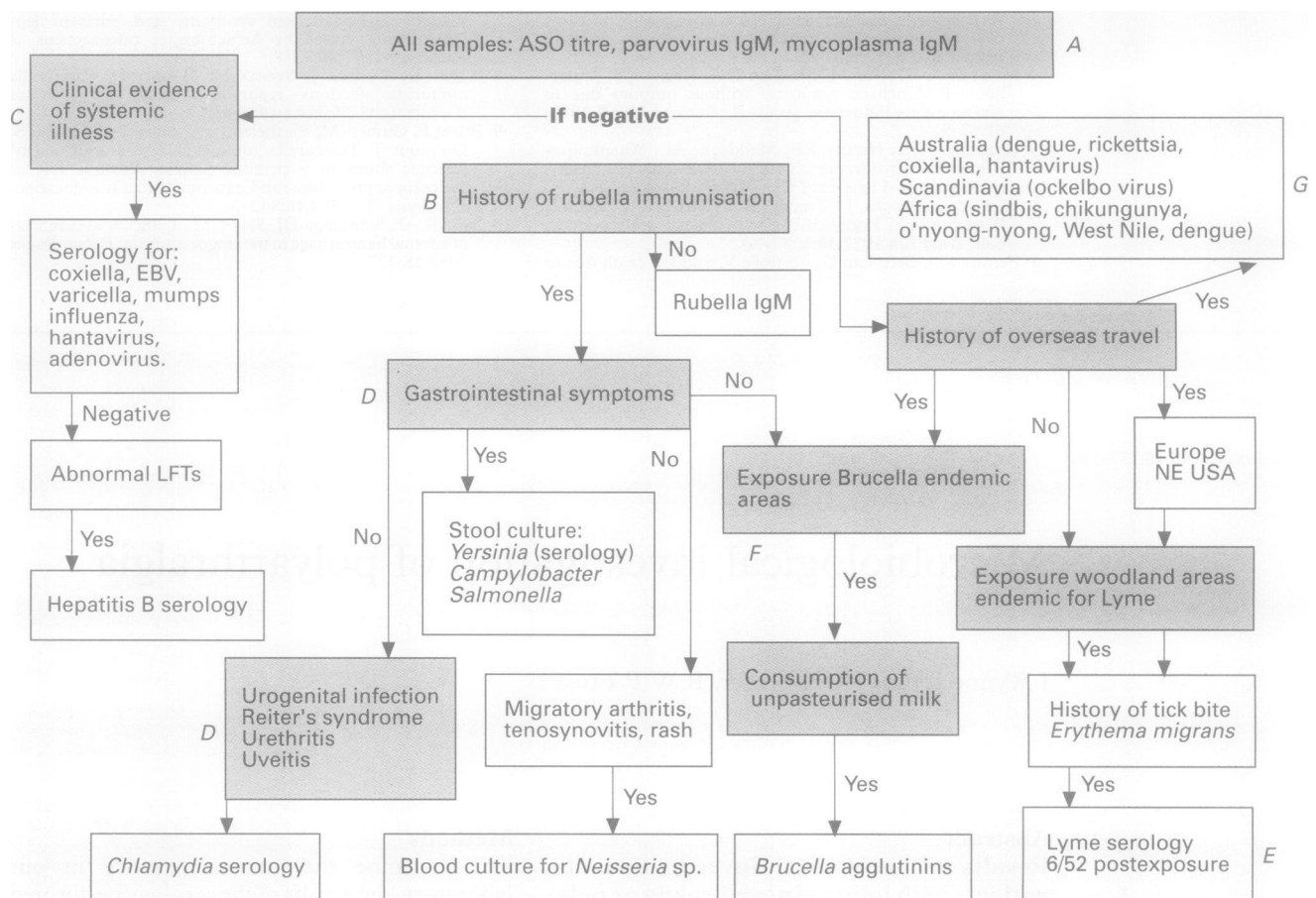
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Tests performed on 140 serum samples submitted for investigation of polyarthralgia

Investigation	Number of samples tested	Number of samples positive (%)
Routine virus screen	117	0
ASO	117	12 (10.3)
Monolateral (heterophil antibodies)	108	10 (9.2)
Rubella IgM (ELISA)	110	1
Mycoplasma IgM (ELISA)	101	2 (1.9)
Parvovirus IgM (radioimmunoassay)	122	35 (28.7)
Lyme serology (ELISA)	18	1

Routine viral CFTs include the following antigens: influenza A and B; adenovirus; respiratory syncytial virus; Q fever; and Psittacosis. Serology tests for *Leptospira* (n=3), *Brucella* (n=2), *Yersinia* (n=2), *Toxoplasma* (n=3), hepatitis B (n=1), and *Chlamydia* (n=2) were also performed with negative results.



Algorithm for the microbiological investigation of polyarthralgia.

All of the serum samples were examined for rubella IgM. The single rubella positive IgM result was observed in a serum simultaneously exhibiting a mycoplasma IgM titre and a positive monolateral test, so this was presumably a non-specific response. No evidence of recent viral infection was obtained from the routine complement fixation tests (CFTs) performed. On the basis of these results, it was concluded that the rubella IgM, monolateral test for heterophil antibodies and the general screen for viral infection (CFT) could be reasonably omitted from the primary screen.

Discussion

A schematic representation of the algorithm is presented in the figure.

A—The algorithm incorporates a group of three primary tests performed on all serum samples: ASO titre, parvovirus IgM and mycoplasma IgM which, respectively, accounted for 12, 35 and one of the 49 significant results in our series. Poststreptococcal illness can range from minimal arthralgia to severe migrating arthritis of acute onset.⁴ With the probable resurgence of streptococcal disease, investigation of all cases for evidence of recent streptococcal infection is warranted.⁴ Until recently, rubella infection was a well known cause of viral polyarthritides but the increasing prevalence of rubella immunisation has led to the virtual disappearance of this infection and the emergence of parvovirus, particularly in epi-

demic waves, as one of the primary causes of viral polyarthritides in the community.^{5,6} Twenty nine of the 35 patients with parvovirus induced polyarthritides were from the community; 30 were women and 21 were between 30 and 50 years old. Only 12 (33.3%) of the requests from patients positive for parvovirus IgM mentioned the presence of a rash and 16 (45.7%) indicated the duration of polyarthritides, which varied from under 14 days in 13 patients to six months in one patient.

Mycoplasma IgM has been included in the primary tests despite the low prevalence during our study because it is a well recognised cause of polyarthralgia and the incidence of *Mycoplasma pneumoniae* changes from year to year. When these primary tests are negative, additional investigations are initiated after completion of a clinical questionnaire eliciting supplementary information.

B—It is no longer necessary to screen all serum samples for rubella IgM without obtaining information on the immunisation status.

C—Polyarthralgia can be a rare sequel to infection with EBV, rickettsia, coxiella (Q fever), varicella, Coxsackie B virus, mumps, adenovirus, and ECHO viruses, but without evidence of recent systemic illness or suggestive clinical findings, routine investigation does not appear to be indicated. It must also be kept in mind that patients with hepatitis B may have polyarthralgia with fever and sometimes have a rash that precedes the onset of hepatitis which resolves when jaundice is evident.¹

D—Reactive polyarthritis, including Reiter's syndrome, develops following infection and is a mild to severe migratory asymmetrical aseptic polyarthritis mainly affecting the large joints.⁷ The condition most commonly follows gastroenteritis caused by *Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia*, or urogenital infection caused by *Chlamydia trachomatis*.⁷ The diagnosis is preferably confirmed by isolation of the causative micro-organism. Post-chlamydial arthralgia, however, can be successfully diagnosed by demonstration of the group (CFT) antibody and confirmed by detection of the type specific antibody by immunofluorescence. *Yersinia* serology is also available but isolation of the organism is more satisfactory.

E—Reactive migratory arthritis exhibiting little joint swelling also occurs in Lyme disease. The diagnosis is difficult because of the six or more weeks delay in appearance of detectable antibody.⁸ Serology is only undertaken when there is a clinical history suggestive of erythema migrans or possible exposure to tick bites.

F—In the past brucellosis was an established cause of arthritis but the cases reported annually to the Communicable Disease Surveillance Centre, London, have declined from 271 in 1972 to 16 in 1992, with nine infections acquired abroad. Therefore, investigation for *Brucella* agglutinins is only undertaken when there is a history suggestive of exposure.

G—No travel history was obtained from any of the cases in this series. In the past, however, polyarthritis following Ross River Valley Fever, Ockelbo, West Nile, and Sindbis viral infections has been diagnosed in this laboratory after travel abroad.⁹ To ensure such cases are not overlooked, a travel component was incorporated in the algorithm.

An awareness that in certain geographical areas rodent borne, aerosol spread virus infections can cause polyarthralgia led to the recent observations in this country of the symptom complex reported in association with hantavirus infection.¹⁰ The infection is relevant in rural areas particularly when there is a history of possible exposure to rodents.

The application of this algorithm to the investigation of arthralgia will assist in selection of the appropriate tests while keeping unhelpful tests to a minimum. A total of 753 individual tests were carried out in this series. If the rubella IgM (£7.76)*, the monolateral test (£0.99)* and screening for viral infection (£7.44)* are omitted from the initial battery of tests, 335 (44.4%) fewer investigations are required with a possible saving of £740.

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* These prices were obtained from a preliminary costing exercise.

Fatal adenovirus 32 infection in a bone marrow transplant recipient

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Abstract

A case of disseminated adenovirus type 32 infection causing severe hepatitis, gastrointestinal ulceration and also with respiratory involvement is reported in a bone marrow transplant recipient. Typical viral inclusions were seen in the postmortem histological sections and adenovirus infection was confirmed using in situ hybridisation and isolation of adenovirus type 32 from separate organs at necropsy. This is the first case in which adenovirus 32 was the cause of fatal disseminated dis-

ease in a bone marrow transplant recipient.

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Keywords: Adenovirus, bone marrow transplant, in situ hybridisation.

Adenovirus infections are well recognised as a cause of serious morbidity and mortality in immunocompromised patients¹ and have been reported in renal,² liver,³ and bone marrow transplant recipients.^{4,5} The complications include hepatitis, pancreatitis,⁶ bowel in-